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Award Number: W81XWH-10-1-0459

TITLE: Collaborative Undergraduate HBCU Student Summer Training Program Award

PRINCIPAL INVESTIGATOR: David Lubaroff

CONTRACTING ORGANIZATION: University of Iowa, Iowa City, IA 52242

REPORT DATE: June 2011

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	**2. REPORT TYPE**	**3. DATES COVERED** *(From - To)*
01-06-2011	Annual	1 JUN 2010 - 31 MAY 2011

4. TITLE AND SUBTITLE

Collaborative Undergraduate HBCU Student Summer Training Program Award

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-10-1-0459

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

David Lubaroff

E-Mail: david-lubaroff@uiowa.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

University of Iowa, Iowa City, IA 52242

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The HBCU Summer Research Training Program accepted a total of 17 students from Lincoln University for the eight week session during the summers of 2010 and 2011. Each student was assigned to a laboratory of a participating mentor and also paired with a member of the mentor's laboratory. This laboratory member assisted with day to day aspects of the research project. During the summer the students worked diligently on their research project, participated in meetings of the mentor's laboratory, attended workshops and seminars associated with our and other summer programs, and attended a special course in prostate cancer. We integrated the Lincoln students into social programs held throughout the campus for summer interns and they attended and participated in the CIC Conference at the Ohio State University in 2010. At the end of the summer sessions the students presented a poster of the research results from the summer experience. They also presented the results of their research in the fall at Lincoln University. Of the students that have graduated from Lincoln, approximately 75% are attending postgraduate programs.

15. SUBJECT TERMS

Summer research; prostate cancer; HBCU institutions

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
U	U	U	UU	21	**19b. TELEPHONE NUMBER** *(include area code)*

Introduction:

The original grant, awarded in 2006, supported five students per summer and a second grant, awarded in 2007, supported three additional students to allow our program to train eight students each year. Although this award was for a renewal of the second grant for additional students I am submitting the annual report on the entire summer training program that includes both of the grant awards. For the year reported here we had the following faculty participants: David M. Lubaroff, PhD, Principal Investigator, Paul Heidger, PhD, University of Iowa Faculty Advisor, Derek Swinton, PhD, Lincoln University Faculty Advisor, and the following mentors: Jackie Bickenbach, PhD, Andrean Burnett-Simons, PhD, Elizabeth Chrischilles, PhD, Frederick Domann, PhD, Elizabeth Field, MD, Thomas Griffith, PhD, Michael Henry, PhD; Siegfried Janz, MD, Yi Luo, MD, PhD, Aliasger Salem, PhD, Michael Schultz, PhD, Douglas Spitz, PhD, George Weiner, MD, Michael Wright, PhD, and Nicholas Zavazava, MD.

Body:

Recruitment and Admission:
Brochures, application forms, and posters were designed and printed and sent to Dr. Swinton at Lincoln and one of the faculty mentors PI traveled to Lincoln University in February 2009 and January 2010, met with Dr. Swinton, Dr. John Chikwem, and the Chairmen of the Departments of Chemistry and Biology. Presentations were made about the summer training program to three groups of students at the beginning of their classes. Nineteen applications were received for the 2010 summer session and 16 for the 2011 summer sessio. The applications were reviewed by the Admissions Committee whose membership consisted of Dr. Lubaroff, Dr. Heidger, Dr. Henry, Dr. Domann, and Dr. Swinton. After making offers to students admission was offered to a total of ten students for the summer of 2010 and eight students for the summer of 2011. In 2011 one of the students retracted their acceptance for personal reasons.

Students Participating in the 2010 Program:
Theresa Akede
Christiana Awoyemi
Kaylene Baugh
Nakita Brown
Chalwe Diallo
Danielle Holsey
Jhanelle Marks
Danielle McKnight
Stephanie Rand
Stephen Sangster

Students Accepted for the 2011 Program
Jhoneil Cooper
Darah Doubt-Swinton
Jodi-Ann Foster
Patrick Ihejirika
Candice Lynch
Ayanna Raeburn
Nathaniel Sangster

Advance Preparation and Information Distribution:
Following acceptance of the students into the program we assigned each student a mentor based upon his/her choices listed in their applications. Each mentor then assigned a member of the lab as a "big brother/big sister," a person that partners with the student during the 8 week summer session. The mentor also prepared a portfolio of articles covering the area of research the student would be working on, including published papers by the mentor. These materials were sent to the students in advance of their arrival at the University of Iowa.

A six week course on Prostate Cancer was organized with six faculty assigned to deliver lectures. The following represents the course schedule with lecturers:

Iowa-Lincoln Summer Research Training Program – 2010
Prostate Cancer Course
9:00am – 10:00am
Room 3240 MERF

Lecture	Date	Subject	Lecturer
Week 1	June 15	Epidemiology of prostate cancer	Dennis
Week 2	June 22	Introduction to cancer	Spitz
Week 3	June 29	Basic aspects of prostate cancer	Dahmoush
Week 4	July 6	Genetics of prostate cancer	Domann
Week 5	July 13	Clinical treatment of prostate cancer	Vaena
Week 6	July 20	Immunotherapy of prostate cancer	Lubaroff

The course planned for the summer of 2010:

Iowa-Lincoln Summer Research Training Program - 2011
Prostate Cancer Course
Room 3240 MERF

Lecture	Date	Subject	Lecturer
Week 1	June 14	Introduction to cancer	Spitz
Week 2	June 21	Basic aspects of prostate cancer	Dahmoush
Week 3	June 28	Epidemiology of prostate cancer	Singh
Week 4	July 5	Genetics of prostate cancer	Domann
Week 5	July 12	Clinical treatment of prostate cancer	Vaena
Week 6	July 19	Immunotherapy of prostate cancer	Lubaroff

Housing and meal plans were arranged in collaboration with the Iowa Biosciences Advantage Program (IBA). Lincoln students were paired with IBA students in the dormitory. Plans were also formulated to integrate workshops, lectures, and social events with other programs dedicated to the training of minority students, such as the Iowa Alliance for

Graduate Education and Professiorate (AGEP), CIC Iowa Summer Research Opportunities Program (SROP), and Iowa Biosciences Advantage (IBA) Program.
Program web sites:
IBA: http://www.uiowa.edu/iba
AGEP: http://www.agep.iastate.edu
SROP: http://www.grad.uiowa.edu/students/SROP

The Summer Program:
A welcoming summer picnic was held on the day of the student's arrival in Iowa City in conjunction with the other summer programs at the University of Iowa. The following day the students wet with the PI, administrator, mentors, and big brothers/sisters for an orientation and then taken to the laboratory of their mentors to begin the summer research training program.

During the 8 week session each student worked diligently with his/her mentor and lab partner on the assigned research project. Each student had an independent project. They attended seminars, workshops, lab meetings, journal clubs and the weekly lectures in the program's prostate cancer course (see schedule above). During the seventh week the PI met individually with each student to evaluate his/her summer experience. The unanimous opinion was that the program was a success. The students indicated that they learned much about research, about prostate cancer, and about the advantages of a research career. At the end of the summer session each student presented their research as part of a poster session held during an afternoon of the last week. In addition to the poster presentations each student gave an oral summary of their research project to the mentors, big brothers/sisters, and other summer students. In addition to the mentoring the students received from their research lab and the PI, they received career counseling. We discussed the options for each of them based upon their experience and their desire for the type of future they envisioned for themselves. Among the topics discussed was graduate school versus medical school, their ultimate goals of research, patient care, and/or teaching.

All of the students attended the CIC Conference held July 23-25, 2010 at the Ohio State University, Columbus, OH. Each student presented a poster of their research and participated in roundtable discussions with students from other CIC-associated institutions. Dr. Heidger accompanied the students on the trip. The students did not attend the 2011 conference since it was scheduled for an earlier date and there would have been insufficient time for their research to yield significant results.

Follow-Up:
We made frequent contact with all of the students after their departure from the University of Iowa. The mentors, faculty advisors (Heidger and Swinton), and mentors, all had contact with the students since the end of the 2006 summer session. Many of the mentors were asked to write letters of reference for the students' applications to graduate schools. The following table reports on the current status of the 2006, 2007, 2008, 2009, and 2010 summer students.

Lincoln Student Follow-Up

Name	Year	Lab	School	Program or Current Year at Lincoln
Oluwaseun Adekanye	2006	Griffith	Penn State	medical school
Shaynah Browne	2006	Lubaroff	U. Mass	graduate school
Nikesha Haynes	2006	Henry	U. Rochester	graduate school
Shivaughn Johnson	2006	Field	Ross University Medical School	medical school; left and working
Briquel Sherman	2006	Zavazava	University of West Indies	medical school
Shaan Spence	2006	Domann	U. South Florida	graduate school
Bisola Awoyemi	2007	Henry	Univ. of the District of Columbia	obtained MS degree, currently working in lab at Harvard.
Seme Diallo	2007	Zavazava	Drexel University	graduate
Caroline Dias	2007	Chrischilles	none at this time	working & applying to grad schools
Titilope Idowu	2007	Domann	Morehouse College	graduate school (public health)
Patrick Ndungu	2007	Lubaroff	University of Iowa	graduate school
Elizabeth Okyne	2007	Spitz	U. Iowa	will enter MPH program at Iowa
Katrina Probherbs	2007	Lutgendorf	Adelphi University	graduate school
Bukola Fatunmbi	2008	Salem	U. Mass	graduate school
Katherine Foster	2008	Spitz	Fox Chase Cancer Center	working
Theon Francis	2008	Field	none at this time	teaching science
Michelle Gray	2008	Lubaroff	Johns Hopkins	working in laboratory
Julia Greenfield	2008	Henry	U. Maryland	graduate school
Gladys Murage	2008	Domann	U. Mass	graduate school
Brittany Stokes	2008	Griffith	none at this time	plans are for Americorp then med school
Stacy-Ann Wright	2008	Bickenbach	Lincoln	senior
Kaylene Baugh	2009	Janz	U. Pennsylvania	research internship
Christina Chisolm	2009	Weiner	U. Mass	graduate school
Seme Diallo	2009	Bickenbach	see 2007	see 2007
Elizabeth Okyne	2009	Spitz	see 2007	see 2007
Stephen Sangster	2009	Domann	none at this time	working; will apply to graduate school for 2012
Keyana Tyree	2009	Salem	U. Mass	graduate school
Neja White	2009	Schultz	none at this time	working at local hospital and apply for medical school for 2012
Akede, Theresa	2010	Luo	Lincoln	senior
Awoyemi, Christiana	2010	Henry	Cameron	junior
Sangster, Stephen	2010	Janz	none at this time	working; will apply to graduate school for 2012
Rand, Stephanie	2010	Weiner	Thomas Jefferson	medical school
McKnight, Danielle	2010	Spitz	Lincoln	senior
Markes, Jhanelle	2010	Schultz	Lincoln	senior
Holsey, Danielle	2010	Salem/Lubaroff	Lincoln	senior
Diallo, Chalwe	2010	Wright	Lincoln	sophomore
Brown, Nakita	2010	Spitz	U. Pittsburgh	post baccalaureate program
Baugh, Kaylene	2010	Lubaroff	see 2009	see 2009

As is evident from the table, of the students that have graduated from Lincoln, 21 of the 29 (72.4%) are attending postgraduate programs (post-baccalaureate, graduate or medical). An additional 5 or 17.2% have plans to apply for postgraduate programs. If these 5 students are successful in entering these programs we will have total of 88.4% of the graduated students continuing their education. This is an amazing statistic. Of the students still enrolled at Lincoln all have applied for other summer research programs for the summer of 2011. One of our former students, Ms. Nikesha Haynes, was highlighted at the 2011 IMPaCT conference as evidence of the success of the HBCU Summer Research Training Program in Prostate Cancer. She is a graduate student at the University of Rochester.

Key Research Accomplishments

Each of the students worked on research projects that were part of an overall program within the laboratory of their mentors. As such, it is difficult to identify key research accomplishments for each student research project. Continuation of the research program by each mentor will certainly produce important research findings, aided in part by the summer research of the Lincoln University students. What is key is the mentoring and counseling of the students to aid in their future as scientists in the area of prostate cancer research. The high percentage of the students that are graduate programs or medical schools is an outstanding accomplishment as these future scientists will most certainly provide key research accomplishments in the years to come.

Reportable Outcomes:

Although the students have not produced any publications from there 8 week research program, they have reported their findings to the University of Iowa faculty, to the faculty and students at Lincoln University, at national competitions and conferences.

Conclusion

The first year of this award was highly successful as evidenced by the amount of work accomplished by each student and by their motivation to continue in a science career. The PI applied, and received funding, for a second HBCU training grant that will enable us to accept additional students for the next 3 years, thus increasing the number of African American scientists in the area of prostate cancer.

Appendices: Brochures for 2010 and 2011

University of Iowa Health Care

Holden Comprehensive Cancer Center

LINCOLN UNIVERSITY
Of the Commonwealth of Pennsylvania

2010
Prostate Cancer Research Summer Training Program

A Collaboration Between the University of Iowa and Lincoln University of Pennsylvania

Students in the 2009 Program

Summary of Program: The partnership of the University of Iowa and Lincoln University is designed to provide an outstanding atmosphere to train undergraduate students from Lincoln in prostate cancer research. We propose to have fourteen mentors available for each of the trainees to choose for their summer research project. The mentors are from seven departments and three colleges at the University of Iowa and the prostate cancer research in their laboratories covers a wide area of interest. The proposed mentors have extensive training experience at all levels; undergraduate, graduate, medical, and postdoctoral.

In addition to the 14 faculty mentors both the University of Iowa and Lincoln University have designated Faculty Advisors for the students. Dr. Paul Heidger serves as the advisor at the University of Iowa and Dr. Derrick Swinton serves as the advisor at Lincoln University. Both individuals are available for advice and assistance throughout the summer and the regular academic year. The faculty members are listed below as well as a brief description of research in the laboratories of each University of Iowa mentor.

At this point in time the program is 8 weeks long, beginning on Monday, June 7, 2010 and ending on Friday, July 30, 2010.

Faculty Advisor at Lincoln University: **Derrick Swinton, PhD.;** Associate Professor, Department of Analytical Chemistry (610- 932-8300, ext.3470)
http://www.lincoln.edu/chemistry/swinton.html

University of Iowa Faculty and Their Research

Director and Research Mentor: **David Lubaroff, PhD**; Professor, Department of Urology & Director of the Summer Research Program (319-335-8423)
http://www.uihealthcare.com/depts/med/urology/urologymds/lubaroff.html

The work in this laboratory concentrates on the area of tumor immunology with an emphasis on immunotherapy. We have constructed microbial vaccines to be used for the investigation of gene and immunotherapy of prostate cancer. Investigations on the ability of immunized animals to produce immune responses to the transgene product induced by the vaccine are underway. Additionally, we are carrying our "translational" research in the form of clinical trials of our adenovirus vaccine in men with prostate cancer. Important in these trials is the safety of the vaccine and its ability to induce anti-tumor immunity. We have recently completed a Phase I clinical trial of the vaccine that demonstrated its safety. Current plans are underway to initiate a therapeutic Phase II trial. Finally, we have been collaborating on studies of psychosocial effects on immune status in cancer patients.

Faculty Advisor: **Paul Heidger, PhD;** Professor, Depat. of Anatomy & Cell Biology (319-335-7722)
http://www.anatomy.uiowa.edu/pages/directory/faculty/heidger.html
Dr. Heidger will assist in the recruitment and evaluation of summer students and will assist in career planning.

Research Mentors

Jackie R. Bickenbach, Ph.D.; Associate Professor, Department of Anatomy & Cell Biology (319-335-6719)
http://www.anatomy.uiowa.edu/pages/directory/faculty/bickenbach.html

The research in the Bickenbach lab involves the understanding of how aging affects keratinocye stem cells and developing molecular mechanisms to de-differentiate and trans-differentiate skin keratinocytes into cells that behave like stem cells, and how cell migration of keratinocytes and cancer cells are affected. Previously, the lab identified a subset of basal skin keratinocytes as stem cells. These cells had multipotent characteristics in that they can differentiate into various other types of cells and tissues. Currently, they are looking for specific markers for these stem cells, and trying to determine whether they have activated different signaling pathways. Of primary interest is whether these stem cells have potential clinical relevance, especially in age-related diseases, particularly cancers. Dr. Bickenbach's lab has shown that the age of the keratinocyte stem cell has little effect on its multipotent capabilities, and thus could be used in translational or clinical cell-based therapies. In another project, the lab is using specific transcription factors to de-differentiate skin keratinocytes into cells that behave similar to stem cells. This translational project produces cells that can be tested in models of human disease.

Elizabeth Chrischilles, Ph.D.; Professor, Department of Epidemiology (319-384-5009)
http://www.public-health.uiowa.edu/epi/faculty/elizabeth_chrischilles.html

Dr. Chrischilles directs the Health Effectiveness Research Center (HERCe) (www.public-health.uiowa.edu/herce/), a collaborative research enterprise between the Department of Epidemiology and the College of Pharmacy at the University of Iowa. HERCe focuses on understanding the reasons for and consequences of treatment variation in clinical practice. It is a center for research, learning, and education that is comprised of epidemiologists, economists, biostatisticians, clinicians, database specialists, geographers, and graduate students from

colleges and departments across campus. Areas of expertise include conceptualization and measurement of preventive care and treatments from retrospective data; methodologies for addressing treatment selection bias including instrumental variables and direct statistical and design control for confounding; population-based sampling; analysis of complex sample surveys and longitudinal data; geographical analysis of healthcare access; data linkage and application of encryption methodologies to maintain confidentiality; and synthesis of drug information to evaluate medication safety. Examples of HERCe research include recent publications on breast cancer treatments, complications of chemotherapy for lymphoma patients, invasive treatments for acute myocardial infarction, and an evaluation of the Iowa Medicaid Pharmaceutical Case Management program.

Frederick Domann, PhD.; Professor, Dept. of Radiation Oncology. (319-335-8018)
http://www.uihealthcare.com/depts/med/radiationoncology/frrb/faculty/domann.html

The Domann laboratory is predominantly interested in the regulation of gene expression in cancer that does not involve classical changes in the DNA sequence, but rather is mediated through so-called "epigenetic" events. These include DNA methylation, histone modifications that affect DNA accessibility, and chromatin conformational changes that render genes available or unavailable for efficient transcription. During a typical summer research experience the undergraduate student would learn how to develop and test a scientific hypothesis related to a fundamental question in cancer research using state of the art techniques and approaches. Methods learned would include human cell culture, nucleic acid extraction, conventional PCR, reverse-transcriptase-PCR to measure mRNA, real-time quantitative PCR, DNA sequencing, DNA methylation analysis, western blotting, enzyme assays, and molecular cloning. The student would become proficient at the techniques through daily interactions with laboratory staff. In addition, the student would become familiar with the theory behind each technique and interpretation of their laboratory results through twice weekly meetings with Professor Domann. It is the goal of this research experience to allow the student the opportunity to participate in larger ongoing research projects in the lab in a substantive way so that he or she can contribute to a publication

Elizabeth H. Field, M.D.; Professor, Department of Internal Medicine (319-339-7078)
http://www.int-med.uiowa.edu/Divisions/Rheumatology/Directory/ElizabethField.html

CD4+CD25+ T regulatory (Treg) lymphocytes are both beneficial and deleterious to health, maintaining tolerance to autoantigens and alloantigens on the one hand while preventing immunity to tumor or pathogens on the other. Because of their dual effect it is important to define their mechanism of action. The Field laboratory utilizes four dimensional live cell imaging and fluorescent fusion proteins to probe the functional interactions of CD4+CD25+ regulatory cells. Because CD4+CD25+ Treg cell activity require cell:cell contact, IL-2, and CD25, one project defines the dynamic processes involved in the paracrine delivery of IL-2 to Treg cells. The lab generates various IL-2 and CD25 fluorescent fusion proteins and expresses these in live cells to image IL-2 and CD25 intra- and intercellular trafficking profiles and dynamic protein:protein interactions between cells. Other projects characterize the dynamic and functional interactions of CD4+CD25+ T regulatory and conventional CD4+ cells or dendritic cells in a model of skin inflammation and a mouse model of HPV cancer.

Thomas Griffith, PhD; Associate Professor, Department of Urology (319 335 7581)
http://www.uihealthcare.com/depts/med/urology/urologymds/griffith.html

The research in the Griffith laboratory studies the therapeutic potential of apoptotic cell death in the treatment of cancer. The tumor necrosis family member TRAIL/Apo-2 ligand is a potent inducer of tumor cell apoptosis, but is non-toxic against normal cell and tissues, suggesting that TRAIL might be administered as an antitumor therapeutic without the side effects seen with other TNF family members, namely TNF and Fas ligand, and traditional chemotherapeutics. Employment of various gene delivery systems, such as non-replicative viral vectors, is making it possible to administer genes directly into tumors sites in situ. Using this technology, a recombinant, replication-deficient adenoviral vector encoding the full-length TRAIL cDNA (Ad-TRAIL) was developed in the laboratory as a way to induce tumor cell death. Current experiments are investigating the ability of Ad-TRAIL to activate systemic antitumor immunity. Additional studies are investigating the role of the innate immune system, specifically neutrophils, in the anti-tumor response activated by Mycobacterium bovis BCG intravesical therapy for bladder cancer. Recent studies in our laboratory demonstrated that TRAIL is induced by BCG treatment, and TRAIL levels in the urine correlated with effective therapy. Of the leukocytes present in the urine, neutrophils expressed high levels of TRAIL. In vitro, human peripheral blood neutrophils contain large intracellular stores of functional TRAIL that is released after stimulation with BCG. Current studies are investigating the contributions of neutrophils in BCG

therapy for bladder cancer, and examining the mechanisms behind BCG-induced expression of TRAIL by neutrophils

Michael Henry, PhD; Associate Professor, Department of Physiology & Biophysics (319-335-7886)
http://www.physiology.uiowa.edu/faculty/faculty/henry.htm

Research in the Henry laboratory is geared toward understanding the molecular and cellular biology underlying the spread of cancer cells from the prostate to other vital organs such as bone, liver and lung. They have developed animal models of prostate cancer metastasis that employ bioluminescence imaging to visualize metastatic cancer cells in living animals. A summer research project would be to engineer and characterize a prostate cancer cell line for expression of the firefly luciferase gene so that it might be used in our animal models.

Siegfried Janz, MD; Professor, Department of Pathology (319-384-2869)
http://www.healthcare.uiowa.edu/pathology/site/faculty/janz/janz.html

Siegfried Janz' primary research interest concerns mouse models of human B cell and plasma cell neoplasms that are induced by the deregulated expression of the cellular oncogene MYC (c-myc). His laboratory has recently generated gene-insertion mice that mimic three different states of the human genetic alterations. He is now developing genetic methods for the detection of the homologous Myc-activating translocations in mice. As leader of the Cancer Genetics and Computational Biology Program at the Holden Comprehensive Cancer Center, he is also actively engaged in research on human blood cancers.

Yi Luo, MD, PhD; Assistant Professor, Department of Urology (319-335-9835)
http://www.uihealthcare.com/depts/med/urology/urologymds/luo.html

A major research project in our laboratory is to develop a novel therapeutic strategy to cope with the limitations of the current modalities for prostate cancer treatment. We will use prostate-specific antigen (PSA), a protein known to be aberrantly expressed in prostate cancer, as a target for immunotherapy of prostate cancer. In fact, PSA has been demonstrated to be a useful immunotherapeutic target in clinical trials as well as in animal models. In addition, PSA has also been demonstrated to be antigenic and capable of inducing specific immune responses in both humans and mice. However, up to date, all currently available PSA-targeted immunotherapies have only demonstrated limited antitumor effects. To improve this immunotherapeutic approach, we will use both bacillus Calmette-Guérin (BCG, a bacterial vaccine strain) and adenovirus (Ad, a replication-defective strain) to deliver PSA for animal immunization. Both BCG and Ad microbes have been demonstrated to be safe and effective for antigen delivery in humans and mice. Since these two microbes are known to be different in their infectious modes and host anti-infection responses, rationally combined use of BCG and Ad recombinants for vaccination will provide a synergistic/complementary immune induction and thus likely result in enhanced antitumor immunity. Indeed, we have previously observed a robust induction of PSA-specific T cell responses by vaccination with combined BCG-PSA (primer vaccine) and Ad-PSA (booster vaccine) in mice. In this study, we will further evaluate the effects of this vaccination method on preventing or treating experimental prostate tumors. The objective of this study is to provide a proof of principle that enhanced antitumor immunity can be achieved by combined vaccination with BCG and Ad recombinants.

Aliasger K. Salem, PhD; Assistant Professor, Division of Pharmaceutics, College of Pharmacy (319-335-8810)
http://www.pharmacy.uiowa.edu/pharmaceutics/people/Salem.htm

Dr. Salem's research interests are primarily focused on self-assembling systems, the rational design of novel drug and gene delivery systems and on the development of sophisticated scaffolds for tissue-specific regeneration. In tissue engineering, Dr. Salem's laboratory applies microfabrication techniques to novel biomaterials to provide spatial control over tissue formation and to integrate minimally invasive scaffold delivery strategies. In drug/gene delivery, he is currently exploring the synergistic application of degradable particle technology, CpG oligonucleotides and heat shock proteins for generating sustained immunotherapeutic responses against cancer. Dr. Salem's laboratory also collaborates with Dr. Lubaroff on the use of microparticles in association with cancer vaccines fro the induction of strong anti-tumor immune responses and tumor destruction.

Michael Schultz, PhD; Faculty Associate, Department of Internal Medicine (319-356-4159)
http://www.int-med.uiowa.edu/Divisions/Cardiology/Directory/MichaelSchultz.html

Dr. Schultz's laboratory is interested in exploring cell-surface protein expression (e.g., G-coupled protein receptors) that is amplified in specific cancer cell

lines and developing peptide- and RNA-aptamer-based molecular targeting mechanisms for delivering radionuclides specifically to the site of cancerous tissue in the body. Examples of Dr. Schultz's research include the development of novel radiolabeled peptide-analogs of neuropeptide Y (NPY) that are designed to bind with high affinity to neuropeptide Y subtype 2 receptors (Y2). In a second example of Schultz laboratory research, an ribonucleic acid (RNA) compound (known as an aptamer) has been synthesized that binds tightly to a cell surface protein receptor (referred to as PSMA) whose expression is amplified on the surface of prostate cancer cells relative to normal cells. Through the development of a novel chelator derivative, Dr. Schultz and colleagues are able to radiolabel the aptamer for imaging by PET. These exciting imaging agents serve not only as high resolution probes for evaluating the location and extent of disease, but also pave the way for the development of molecularly-guided therapeutic agents that hold promise in the development of curative approaches to these enigmatic cancers.

Douglas Spitz, PhD; Professor, Department of Radiation Oncology (319-335-8001)
http://www.uihealthcare.com/depts/med/radiationoncology/frrb/faculty/spitz.html

Research in the Spitz laboratory is concentrated on the role of free radicals and oxidative events in cancers. For example, combinations of inhibitors of glucose metabolism, 2-deoxy-D-glucose (2-DG), and of hydroperoxide detoxification, dehydroisoandrosterone (DHEA) and L-buthionine sulfoximine (BSO), have been shown to be effective in killing human tumor cells *via* oxidative stress. 2-DG has also been shown to increase radiosensitivity in human cancer cells both *in vitro* and *in vivo* . These results have led us to test the ability of 20 mM 2-DG + 300 μM DHEA + 1 mM BSO to induce radiosensitization following exposure to 4 Gy ionizing radiation. Clonogenic survival was used as the parameter indicative of cytotoxicity. Prostate cancer cells (PC-3) treated with 2-DG or DHEA alone as well as the combinations of 2-DG + DHEA, 2-DG + BSO, DHEA + BSO, or 2-DG + DHEA + BSO all demonstrated some degree of radiosensitization, and the effect was most pronounced in the group treated with 2-DG + DHEA + BSO, relative to the other combinations (< 2% survival in the 2-DG + DHEA + BSO group versus > 5% with other agents). In another human prostate cancer cell line, DU145, 2-DG + DHEA + BSO also resulted in substantially enhanced radiosensitization when compared to any of the other combinations. These results support the hypothesis that the combining inhibitors of glucose metabolism with inhibitors of hydroperoxide detoxification increases radiation sensitivity in human cancer cells.

George Weiner, MD; Professor, Department of Internal Medicine and Director, Holden Comprehensive Cancer Center (319-353-8620)
http://www.int-med.uiowa.edu/Divisions/HemOnc/Directory/GeorgeWeiner.html

The laboratory of Dr. George Weiner focuses on exploring methods to enhance the efficacy of monoclonal antibody therapy of cancer. Preclinical and clinical studies are exploring the relative role of various effector cells in antibody dependent cellular cytotoxicity, how complement impacts on the efficacy of monoclonal antibody therapy and how therapy can be improved. Dr. Weiner's laboratory is also evaluating the use of other immunotherapy agents such as immunostimulatory CpG oligodeoxynucleotides (CpG ODN). He works closely with Dr. Brian Link who leads the clinical research aspects of their collaborative research program. Dr. Weiner is the Director of the University of Iowa Holden Comprehensive Cancer Center, and of the Iowa/ Mayo Clinic Specialized Program of Research Excellence (SPORE) in lymphoma. He is also the principal investigator of additional research grants from the National Cancer Institute and the Leukemia and Lymphoma Society in the field of immunotherapy of cancer.

Nicholas Zavazava, MD, PhD; Professor, Department of Internal Medicine (319-384-6577)
http://www.healthcare.uiowa.edu/InternalMedicine/Divisions/Allergy/Directory/NicholasZavazava.html

Research in the Zavazava laboratory is devoted to the characterization of primate embryonic stem cells. The motivation for this emphasis is that cancer appears to originate from cancer stem cells. These cancer cells have not been well characterized, but appear to share basic characteristics with embryonic stem cells, for example the property of uncontrolled growth. Characterization of these cells will some day lead to better treatment of cancer. Our laboratory is interested in characterizing primate embryonic stem cells and understanding their properties that allow self renewal and immune evasion. Further, the lab is interested in differentiating these cells in vitro into T cells that could be used for the treatment of cancer in the in vivo situation.

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For additional information please contact one of the following:

David Lubaroff, PhD, Department of Urology, University of Iowa, 375 Newton Road, 3210 MERF, Iowa City, IA 52242; 319-335-8423; david-lubaroff@uiowa.edu

Paul Heidger, PhD, Department of Anatomy & Cell Biology, University of Iowa, 51 Newton Road, Iowa City, IA 52242; 319-335-7722; paul-heidger@uiowa.edu.

Derrick Swinton, PhD, Department of Analytical Chemistry, Lincoln University, 1570 Baltimore Pike, Lincoln University, PA 19352; 610-932-8300, ext. 3470; dswinton@lincoln.edu

Diane Morman, Program Coordinator, Department of Urology, University of Iowa, 375 Newton Road, 3209 MERF, Iowa City, IA 52242; 319-335-8425; diane-morman@uiowa.edu

UNIVERSITY of IOWA HEALTH CARE

Holden Comprehensive Cancer Center

University of Iowa Health Care

Holden Comprehensive Cancer Center

LINCOLN UNIVERSITY
Of the Commonwealth of Pennsylvania

2011
Prostate Cancer Research Summer Training Program

A Collaboration Between the University of Iowa and Lincoln University of Pennsylvania

Students in the 2010 Program

Summary of Program: The partnership of the University of Iowa and Lincoln University is designed to provide an outstanding atmosphere to train undergraduate students from Lincoln in prostate cancer research. We propose to have fourteen mentors available for each of the trainees to choose for their summer research project. The mentors are from seven departments and three colleges at the University of Iowa and the prostate cancer research in their laboratories covers a wide area of interest. The proposed mentors have extensive training experience at all levels; undergraduate, graduate, medical, and postdoctoral.

In addition to the eleven faculty mentors both the University of Iowa and Lincoln University have designated Faculty Advisors for the students. Dr. Paul Heidger serves as the advisor at the University of Iowa and Dr. Derrick Swinton serves as the advisor at Lincoln University. Both individuals are available for advice and assistance throughout the summer and the regular academic year. The faculty members are listed below as well as a brief description of research in the laboratories of each University of Iowa mentor.

At this point in time the program is 8 weeks long, beginning on Monday, June 6, 2011 and ending on Friday, July 29, 2011.

Faculty Advisor at Lincoln University: **Derrick Swinton, PhD.;** Associate Professor, Department of Analytical Chemistry (610- 932-8300, ext.3470)
http://www.lincoln.edu/chemistry/swinton.html

University of Iowa Faculty and Their Research

Director and Research Mentor: **David Lubaroff, PhD**; Professor, Department of Urology & Director of the Summer Research Program (319-335-8423)
http://www.uihealthcare.com/depts/med/urology/urologymds/lubaroff.html

The work in this laboratory concentrates on the area of tumor immunology with an emphasis on immunotherapy. We have constructed microbial vaccines to be used for the investigation of gene and immunotherapy of prostate cancer. Investigations on the ability of immunized animals to produce immune responses to the transgene product induced by the vaccine are underway. Additionally, we are carrying our "translational" research in the form of clinical trials of our adenovirus vaccine in men with prostate cancer. Important in these trials is the safety of the vaccine and its ability to induce anti-tumor immunity. We have recently completed a Phase I clinical trial of the vaccine that demonstrated its safety. We have initiated a therapeutic Phase II trial. Finally, we have been collaborating on studies of psychosocial effects on immune status in cancer patients.

Faculty Advisor: **Paul Heidger, PhD;** Professor, Depat. of Anatomy & Cell Biology (319-335-7722)
http://www.anatomy.uiowa.edu/personnel.shtml?id=heidgerp

Dr. Heidger will assist in the recruitment and evaluation of summer students and will assist in career planning.

Research Mentors

Jackie R. Bickenbach, Ph.D.; Professor, Department of Anatomy & Cell Biology (319-335-6719)
http://www.anatomy.uiowa.edu/personnel.shtml?id=bickenbachj

The research in the Bickenbach lab involves the understanding of how aging affects keratinocye stem cells and developing molecular mechanisms to de-differentiate and trans-differentiate skin keratinocytes into cells that behave like stem cells, and how cell migration of keratinocytes and cancer cells are affected. Previously, the lab identified a subset of basal skin keratinocytes as stem cells. These cells had multipotent characteristics in that they can differentiate into various other types of cells and tissues. Currently, they are looking for specific markers for these stem cells, and trying to determine whether they have activated different signaling pathways. Of primary interest is whether these stem cells have potential clinical relevance, especially in age-related diseases, particularly cancers. Dr. Bickenbach's lab has shown that the age of the keratinocyte stem cell has little effect on its multipotent capabilities, and thus could be used in translational or clinical cell-based therapies. In another project, the lab is using specific transcription factors to de-differentiate skin keratinocytes into cells that behave similar to stem cells. This translational project produces cells that can be tested in models of human disease.

Elizabeth Chrischilles, Ph.D.; Professor, Department of Epidemiology (319-384-5009)
http://www.public-health.uiowa.edu/faculty-staff/faculty/directory/faculty-detail.asp?emailAddress=e-chrischilles@uiowa.edu

Dr. Chrischilles directs the Health Effectiveness Research Center (HERCe) (www.public-health.uiowa.edu/herce/), a collaborative research enterprise between the Department of Epidemiology and the College of Pharmacy at the University of Iowa. HERCe focuses on understanding the reasons for and consequences of treatment variation in clinical practice. It is a center for research, learning, and education that is comprised of epidemiologists, economists, biostatisticians, clinicians, database

specialists, geographers, and graduate students from colleges and departments across campus. Areas of expertise include conceptualization and measurement of preventive care and treatments from retrospective data; methodologies for addressing treatment selection bias including instrumental variables and direct statistical and design control for confounding; population-based sampling; analysis of complex sample surveys and longitudinal data; geographical analysis of healthcare access; data linkage and application of encryption methodologies to maintain confidentiality; and synthesis of drug information to evaluate medication safety. Examples of HERCe research include recent publications on breast cancer treatments, complications of chemotherapy for lymphoma patients, invasive treatments for acute myocardial infarction, and an evaluation of the Iowa Medicaid Pharmaceutical Case Management program.

Frederick Domann, PhD.; Professor, Dept. of Radiation Oncology. (319-335-8018)
http://www.uiowa.edu/~frrbp/domann_lab.html

The Domann laboratory is predominantly interested in the regulation of gene expression in cancer that does not involve classical changes in the DNA sequence, but rather is mediated through so-called "epigenetic" events. These include DNA methylation, histone modifications that affect DNA accessibility, and chromatin conformational changes that render genes available or unavailable for efficient transcription. During a typical summer research experience the undergraduate student would learn how to develop and test a scientific hypothesis related to a fundamental question in cancer research using state of the art techniques and approaches. Methods learned would include human cell culture, nucleic acid extraction, conventional PCR, reverse-transcriptase-PCR to measure mRNA, real-time quantitative PCR, DNA sequencing, DNA methylation analysis, western blotting, enzyme assays, and molecular cloning. The student would become proficient at the techniques through daily interactions with laboratory staff. In addition, the student would become familiar with the theory behind each technique and interpretation of their laboratory results through twice weekly meetings with Professor Domann. It is the goal of this research experience to allow the student the opportunity to participate in larger ongoing research projects in the lab in a substantive way so that he or she can contribute to a publication

Michael Henry, PhD; Associate Professor, Department of Physiology & Biophysics (319-335-7886)
http://www.physiology.uiowa.edu/henry.shtml?menu=1&tab=facultyTab

Research in the Henry laboratory is geared toward understanding the molecular and cellular biology underlying the spread of cancer cells from the prostate to other vital organs such as bone, liver and lung. They have developed animal models of prostate cancer metastasis that employ bioluminescence imaging to visualize metastatic cancer cells in living animals. A summer research project would be to engineer and characterize a prostate cancer cell line for expression of the firefly luciferase gene so that it might be used in our animal models.

Siegfried Janz, MD; Professor, Department of Pathology (319-384-2869)
http://www.healthcare.uiowa.edu/pathology/site/faculty/janz/janz.html

Siegfried Janz' primary research interest concerns mouse models of human B cell and plasma cell neoplasms that are induced by the deregulated expression of the cellular oncogene MYC (c-myc). His laboratory has recently generated gene-insertion mice that mimic three different states of the human genetic alterations. He is now developing genetic methods for the detection of the homologous Myc-activating translocations in mice. As leader of the Cancer Genetics and Computational Biology Program at the Holden Comprehensive Cancer Center, he is also actively engaged in research on human blood cancers.

Yi Luo, MD, PhD; Associate Professor, Department of Urology (319-335-9835)
http://www.uihealthcare.com/depts/med/urology/urologymds/luo.html

A major research project in our laboratory is to develop a novel therapeutic strategy to cope with the limitations of the current modalities for prostate cancer treatment. We will use prostate-specific antigen (PSA), a protein known to be aberrantly expressed in prostate cancer, as a target for immunotherapy of prostate cancer. In fact, PSA has been demonstrated to be a useful immunotherapeutic target in clinical trials as well as in animal models. In addition, PSA has also been demonstrated to be antigenic and capable of inducing specific immune responses in both humans and mice. However, up to date, all currently available PSA-targeted immunotherapies have only demonstrated limited antitumor effects. To improve this immunotherapeutic approach, we will use both bacillus Calmette-Guérin

(BCG, a bacterial vaccine strain) and adenovirus (Ad, a replication-defective strain) to deliver PSA for animal immunization. Both BCG and Ad microbes have been demonstrated to be safe and effective for antigen delivery in humans and mice. Since these two microbes are known to be different in their infectious modes and host anti-infection responses, rationally combined use of BCG and Ad recombinants for vaccination will provide a synergistic/complementary immune induction and thus likely result in enhanced antitumor immunity. Indeed, we have previously observed a robust induction of PSA-specific T cell responses by vaccination with combined BCG-PSA (primer vaccine) and Ad-PSA (booster vaccine) in mice. In this study, we will further evaluate the effects of this vaccination method on preventing or treating experimental prostate tumors. The objective of this study is to provide a proof of principle that enhanced antitumor immunity can be achieved by combined vaccination with BCG and Ad recombinants.

Aliasger K. Salem, PhD; Associate Professor, Division of Pharmaceutics, College of Pharmacy (319-335-8810)
http://www.pharmacy.uiowa.edu/pharmaceutics/people/Salem.htm

Dr. Salem's research interests are primarily focused on self-assembling systems, the rational design of novel drug and gene delivery systems and on the development of sophisticated scaffolds for tissue-specific regeneration. In tissue engineering, Dr. Salem's laboratory applies microfabrication techniques to novel biomaterials to provide spatial control over tissue formation and to integrate minimally invasive scaffold delivery strategies. In drug/gene delivery, he is currently exploring the synergistic application of degradable particle technology, CpG oligonucleotides and heat shock proteins for generating sustained immunotherapeutic responses against cancer. Dr. Salem's laboratory also collaborates with Dr. Lubaroff on the use of microparticles in association with cancer vaccines fro the induction of strong anti-tumor immune responses and tumor destruction.

Michael Schultz, PhD; Assistant Professor, Department of Radiology (319-356-4159)
http://www.medicine.uiowa.edu/Radiology/faculty-staff/faculty/schultz-michael.html

Dr. Schultz's laboratory is interested in exploring cell-surface protein expression (e.g., G-coupled protein receptors) that is amplified in specific cancer cell lines and developing peptide- and RNA-aptamer-based molecular targeting mechanisms for delivering radionuclides specifically to the site of cancerous tissue in the body. Examples of Dr. Schultz's research include the development of novel radiolabeled peptide-analogs of neuropeptide Y (NPY) that are designed to bind with high affinity to neuropeptide Y subtype 2 receptors (Y2). In a second example of Schultz laboratory research, an ribonucleic acid (RNA) compound (known as an aptamer) has been synthesized that binds tightly to a cell surface protein receptor (referred to as PSMA) whose expression is amplified on the surface of prostate cancer cells relative to normal cells. Through the development of a novel chelator derivative, Dr. Schultz and colleagues are able to radiolabel the aptamer for imaging by PET. These exciting imaging agents serve not only as high resolution probes for evaluating the location and extent of disease, but also pave the way for the development of molecularly-guided therapeutic agents that hold promise in the development of curative approaches to these enigmatic cancers.

Douglas Spitz, PhD; Professor, Department of Radiation Oncology (319-335-8001)
http://www.uiowa.edu/~frrbp/spitz_lab.html

Research in the Spitz laboratory is concentrated on the role of free radicals and oxidative events in cancers. For example, combinations of inhibitors of glucose metabolism, 2-deoxy-D-glucose (2-DG), and of hydroperoxide detoxification, dehydroisoandrosterone (DHEA) and L-buthionine sulfoximine (BSO), have been shown to be effective in killing human tumor cells *via* oxidative stress. 2-DG has also been shown to increase radiosensitivity in human cancer cells both *in vitro* and *in vivo* . These results have led us to test the ability of 20 mM 2-DG + 300 μM DHEA + 1 mM BSO to induce radiosensitization following exposure to 4 Gy ionizing radiation. Clonogenic survival was used as the parameter indicative of cytotoxicity. Prostate cancer cells (PC-3) treated with 2-DG or DHEA alone as well as the combinations of 2-DG + DHEA, 2-DG + BSO, DHEA + BSO, or 2-DG + DHEA + BSO all demonstrated some degree of radiosensitization, and the effect was most pronounced in the group treated with 2-DG + DHEA + BSO, relative to the other combinations (< 2% survival in the 2-DG + DHEA + BSO group versus > 5% with other agents). In another human prostate cancer cell line, DU145, 2-DG + DHEA + BSO also resulted in substantially enhanced radiosensitization when compared to any of the other combinations. These results support the hypothesis that the combining inhibitors of glucose metabolism with inhibitors of hydroperoxide detoxification increases radiation sensitivity in human cancer cells.

George Weiner, MD; Professor, Department of Internal Medicine and Director, Holden Comprehensive Cancer Center (319-353-8620)
http://www.healthcare.uiowa.edu/Labs/Weiner/

The laboratory of Dr. George Weiner focuses on exploring methods to enhance the efficacy of monoclonal antibody therapy of cancer. Preclinical and clinical studies are exploring the relative role of various effector cells in antibody dependent cellular cytotoxicity, how complement impacts on the efficacy of monoclonal antibody therapy and how therapy can be improved. Dr. Weiner's laboratory is also evaluating the use of other immunotherapy agents such as immunostimulatory CpG oligodeoxynucleotides (CpG ODN). He works closely with Dr. Brian Link who leads the clinical research aspects of their collaborative research program. Dr. Weiner is the Director of the University of Iowa Holden Comprehensive Cancer Center, and of the Iowa/ Mayo Clinic Specialized Program of Research Excellence (SPORE) in lymphoma. He is also the principal investigator of additional research grants from the National Cancer Institute and the Leukemia and Lymphoma Society in the field of immunotherapy of cancer.

Michael Wright, PhD; Assistant Professor, Department of Molecular Physiology & Biophysics (319-384-1764)
http://www.physiology.uiowa.edu/wright.shtml?menu=1&tab=facultyTab

The Wright Laboratory is focused on defining the composition, activity, and overall cellular function of protein complexes in higher organisms. We utilize quantitative mass spectrometry as a platform to study protein network dynamics in model experimental systems. One of the major projects is the mapping of androgen receptor signaling networks in androgen receptor-related diseases. We are delineating androgen signaling cascades in hormone-responsive systems with the goal of understanding how aberrant androgen receptor (AR) signaling contributes to the development and progression of the AR-related diseases in human prostate cancer. Another project attempts to define molecular biomarkers in androgen receptor-related diseases. This area involves the identification of protein biomarkers in clinical tissue samples of prostate cancer.. We are using both directed and targeted mass spectrometry workflows to identify and quantify tissue biomarkers in radical prostatectomy samples. The goal of this research is to characterize biomarkers to indolent (e.g. organ-confined) and lethal (e.g. metastatic) forms of CaP. These studies have the potential to define novel diagnostic, prognostic, and therapeutic biomarkers in the management and treatment of high-risk, organ-confined CaP and early-stage, metastatic CaP. We are also developing better proteomic workflows to validate tissue biomarkers in plasma and serum using mass spectrometry-based assays.

Nicholas Zavazava, MD, PhD; Professor, Department of Internal Medicine (319-384-6577)
http://www.int-med.uiowa.edu/Divisions/Immunology/Directory/NicholasZavazava.html

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